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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| COUNTS, GARY W | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Advisory Action | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/582,734 | MENDEL-HARTVIG ET AL. | |
| | Examiner | Art Unit | |
| | Gary W. Counts | 1641 | |

*--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

THE REPLY FILED 27 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on *27 May 2004*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

   (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see attached*.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: *1-4 and 6-35*.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)( PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

## DETAILED ACTION

### Attachment to Advisory Action

Continuation of 5 NOTE: Applicant argues that Dafforn et al fails to teach or suggest a method or device wherein flow is initiated by adding liquid to each zone in such a way that $liquid_{n+1}$ contacts the flow matrix substantially simultaneously with and is transported through the matrix immediately after $liquid_n$, added to the nearest downstream application zone $LZ_n$. Applicant directs Examiner's attention to column 24, lines 22-55 which states "The assay can be conducted by adding a sample suspected of containing HCG at the first opening and simultaneously adding a developer solution containing enzyme substrate at the second opening. During subsequent incubation, HCG bind to the conjugate, the complex carried by the moving developer to the detection zone where it binds, and the bound complex acts on the substrate to produce color at the detection zone when HCG is present in the sample". Applicant contends that Dafforn et al teach that "during subsequent incubation, HCG binds to the conjugate, the complex is carried by the moving developer to the detection zone" (col 24, lines 33-24) and thus, Dafforn et al teach that the HCG-enzyme conjugate complex mixes with the developer prior to arrival of the HCG in the detection zone. This is not found persuasive because it appears that Applicant is trying to assert that two separate liquid fronts are moving toward the detection zone, one containing analyte (i.e. sample), and the other containing the labeled reagent. And that a complex between the analyte and the labeled reagent is not formed prior to both liquid-fronts reaching the detection zone. If this is a correct interpretation of the argument, it is not found persuasive because it is

not on point. The claims are not limited to a method where the labeled reagent is moving in a separate front, i.e. behind a sample liquid. Instead, the claims recite an embodiment where the labeled reactant is located in the same zone where sample is added, (i.e. $LZ_{n"}R^*$ and $LZ_n$ with n" $\geq$ n'), since n is recited as the position of the application zone ($LZ_n$), the indication that n" is $\geq$ n' is interpreted as an embodiment where the sample application zone and the zone for the labeled reactant is the same, i.e. Dafforn, column 24, lines 23-46. In this case, a complex between the analyte and the labeled reactant is formed when sample is added to $LZ_n$, and this complex is moving in front of any liquid that is added to the other liquid addition zones. Because the claims do not make clear what "liquid" may be added to the various zones, this "liquid" could be buffer or substrate solution, in which case, after the complex of Dafforn reaches the detection zone, the bound complex acts on any substrate solution that subsequently enters the detection zone, resulting in a color change. These teachings are seen to be the same as those of the instant claims.

With respect to Applicants arguments that the complex mixes with the developer prior to arrival of the HCG in the detection zone. This is not found persuasive because regardless if the developer is added or not the complex will flow toward the detection zone. Furthermore, there is simply no support for the Applicant's assertion that the complex and developer mix. The addition of developer after the complex would flow behind the complex. Further, as disclosed by Dafforn absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for

analyzing for the analyte (col 4, lines 12-16). Therefore, when sample is applied to application zone downstream of liquid reagent, the sample begins to migrate and therefore even when the sample and liquid reagent are added simultaneously the sample would flow in front of liquid reagent. If the complex and developer were mixed together the reaction would occur before the detection zone. Dafforn clearly states (col 24, lines 35-37) that the reaction occurs at the detection zone. Therefore, the complex binds to the immobilized antibody and then the developer reacts to produce a color change. Thus, Dafforn reads on the instantly recited claims.

Further, with respect to independent claims 1 and 18 as instantly recited. It appears that the claims are missing an essential element for achieving sequential flow without mixing of fluids between the two application zone. On page 6, lines 10-18 of the specification the applicant discloses that "A liquid added in an application zone may have a tendency to spread on top of the matrix to parts of the matrix being outside the zone. For adjacent zones this means that liquids may be mixed with each other in an undesired way. To avoid this, physical barriers delimiting two adjacent application zones (zone spacers) are placed. The barriers should primarily be placed on top of the matrix, but may be extended down into the matrix without completely quenching the flow. Therefore, if applicant maintains that Dafforn et al involves mixing, it is the Examiner's position that since independent claims 1 and 18 do not recite spacers, that applicant's invention would also have mixing occurring. The first recitation of spacers does not occur until claim 10 (see above rejection). Further, as stated above Dafforn teaches spacers as recited in claim 10.

Applicant argues that present claims 1 and 18 still require at least two liquid application zone in which flow is initiated and require that flow is initiated by adding liquid to each zone in such a way that liquid added to an upstream zone $LZ_{n+1}$ contacts the flow matrix substantially simultaneous with and is transported through the matrix immediately after liquid added to the nearest downstream application zone $LZ_n$. Applicant states that according to claims 1 and 18, if n"=n', there is still yet another application zone which meets the requirements of section II of claim 1 and section e of claim 18, which is not taught by Dafforn et al. This is not found persuasive because Dafforn et al specifically teaches two application zones (Fig 1). Dafforn et al discloses that liquid reagent is applied in sample well (22) and sample is applied to sample well (20). Dafforn et al also discloses that the liquid reagent and sample can be applied simultaneously (col 24, lines 23-55). Therefore, the application of liquid reagent and sample at the two application zones would cause flow to be initiated in the two zones. Further, Dafforn et al also teaches additional application zones (see Figures 6-9) added to the device.

Applicant argues that Dafforn does not teach or suggest the flow matrix comprises liquid application zones having zone spacers between each other, i.e., in the flow matrix, rather than in a housing well. This is not found persuasive because instantly recited claims 10 and 24 merely recite wherein the zones $LZ_m..LZ_n..LZ_1$ have zone spacers between each other. One skilled in the art would recognize that the dividers of Dafforn et al are incorporated as part of the flow matrix between the application zones and thus would act as spacers. In response to applicant's argument

that the references fail to show certain features of applicant's invention, it is noted that thee features upon which applicant relies (i.e., in the flow matrix, rather than in a housing well) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns,* 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Therefore, Dafforn reads on the instantly recited claims.

Applicant argues that there is no suggestion by Dafforn et al for modifying their teachings along the lines of the presently claimed methods and devices, nor is there any suggestion by Dafforn et al regarding the desirability of any such modification. This is not found persuasive because as stated in the previous office action Dafforn et al specifically teach that the Reactant* can be applied upstream of the liquid application zone for sample. Dafforn et al also disclose many embodiments regarding Reactant* in which Reactant* is applied upstream of the application zone of sample or to the same zone as the sample. Although, Dafforn teaches that when (Reactant*) is added upstream of sample, that the liquid reagent usually is added following the addition of sample (col 13, lines 32-44), Dafforn also teaches the addition of liquid reagents simultaneously (col 24). Therefore, it would have been obvious to one of ordinary skill in the art to add Reactant* upstream of a liquid application zone for sample and to apply the liquids simultaneously in order to optimize assay conditions.

Applicant argues that the methods and devices defined by claims 12, 115 16, 26, 29 and 30 are nonobvious over and patentably distinguishable from the combination of Dafforn et al and Robinson et al. Applicant specifically argues that there is no

teaching or suggestion by Dafforn et al relating to an additional zone $LZ_{n''}R$ as presently claimed, relating to calibration. This is not found persuasive because Dafforn et al specifically teaches that additional application zones can be implemented into their method and device (Figures 6-9) and one of ordinary skill in the art would recognize that the incorporation of the calibration zones of Robinson et al into the method and device of Dafforn et al would also require the application of the corresponding reagents for the calibrant in the calibration zones. Further, Robinson et al clearly disclose (page 5, lines 7-15) that the device can be a test strip (same as Dafforn) and Robinson clearly states the advantages of using calibration zones and calibration reagents (page 3, lines 15-16 and page 14, lines 24-26). Therefore, it is the Examiner's position that the combination of Dafforn et al and Robinson et al is proper and thus the rejection is maintained.

Applicants argue that the deficiencies of Dafforn et al are not resolved by Self. That is, while Self discloses an immunoassay using an amplified cyclic detection system, Applicants find no teaching or suggestion by Self relating to a method or device for determination of an analyte in a sample and a flow matrix employing a combination of biospecific affinity reactants and liquid application zones and flow as defined in claims 1 and 18. This is not found persuasive Examiner has not relied upon Self for these limitations but rather has relied upon Dafforn et al for these limitations. Further, Dafforn et al specifically teach that the device may be utilized in any number of assay wherein absorbent material is utilized to assist the flow of liquid away from a contact portion where the absorbent material is contacted with a medium containing the analyte to be determined or reagents for analyzing for the analyte (col 4, lines 11-16). Further,

Dafforn et al disclose that the device can be used to detect autoimmune antibodies and antibodies to allergens (col 5, lines 1-6). Since, Self et al disclose that immunoassays are used for the detection and/or determination of autoimmune disease. It is the Examiner's position that it would have been obvious to one of ordinary skill in the art to combine the teachings of Dafforn et al and Self et al.

Applicant argues that the deficiencies of Dafforn et al are not resolved by Goerlach-Graw et al. Applicant argues that Goerlach-Graw does not teach a single flow matrix having liquid application zones in series therein as required in claims 1 and 18. This is not found persuasive because Examiner has not relied upon Goerlach-Graw et al for these limitations but rather has relied upon Dafforn et al. Applicant argues that there is no teaching or suggestion of zone spacers as presently claimed between a series of liquid application zones in a single flow matrix, or for modifying the teachings of Dafforn et al along the lines of the present invention. Applicant argues that such test strips are contrary to promoting contact between developer and conjugate as desired by Dafforn et al. It appears that Applicant is relying upon the previous argument that Dafforn teaches mixing of the developer and the complex. This is not found persuasive because as stated above Dafforn does not teach does not teach mixing of the developer and the complex (see Examiner's response above with respect to Applicants arguments that the complex mixes with the developer prior to arrival of the HCG in the detection zone). Further, Goerlach-Graw specifically teaches the advantages of incorporating such strips into a flow matrix.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary W. Counts
Examiner
Art Unit 1641
June 8, 2004

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08/07/04